REMARKS

Claims are canceled in this Preliminary Amendment for the sole purpose of reducing the filing fees for the application. The claims are canceled without prejudice to or disclaimer of the subject matter thereof, and Applicants expressly reserve the right to pursue such claims in a continuing application.

Attached hereto is a marked up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version With Markings to Show Changes Made." Also, for the convenience of the Examiner and because the number of claims canceled in this Preliminary Amendment is quite large, Applicants have attached a clean version of the entire set of pending claims as set forth in 37 CFR § 1.211(c)(3).

Respectfully submitted,

SHERIDAN ROSS P.C.

By: _____

Gary J. Connell
Registration No. 32,020
1560 Broadway, Suite 1200
Denver, Colorado 80202-5141
(303) 863-9700

Date: June 14, 2002

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

In the Claims:

Claims 2-52, 84-118, 120-123, 125-128, 130-133, 135-157, 159-181, 183-205, 207-233, 263-265, 267-269, 271-292, 294-315, 317-342, 344-369, 371-391, 393-414, and 416 have been cancelled.

82. (Amended) The method of [any one of Claims 53-81] Claim 53 wherein the cell, tissue or organ is transplanted into an animal after being contacted with the solution or medium containing the peptide.

Pending Claims
(Following Entry of Preliminary Amendment)

1. A method of reducing the damage done by reactive oxygen species (ROS) in an animal comprising administering to the animal an effective amount of a peptide having the formula:

$$P_1 - P_2,$$

wherein:

$P_1$ is:

$Xaa_1$ $Xaa_2$ His: or

$Xaa_1$ $Xaa_2$ His $Xaa_3$;

$P_2$ is $(Xaa_4)_n$;

$Xaa_1$ is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_2$ is glycine, alanine, β-alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_3$ is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

$Xaa_4$ is any amino acid; and

n is 0-100;

or a physiologically-acceptable salt thereof.

53. A method of reducing the damage done by reactive oxygen species (ROS) to a cell, a tissue or an organ that has been removed from an animal comprising contacting the cell, tissue or organ with a solution or medium containing an effective amount of a peptide having the formula:

$$P_1 - P_2,$$

wherein:

$P_1$ is:

$Xaa_1$ $Xaa_2$ His: or

$Xaa_1$ $Xaa_2$ His $Xaa_3$;

$P_2$ is $(Xaa_4)_n$;

$Xaa_1$ is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_2$ is glycine, alanine, β-alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_3$ is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

$Xaa_4$ is any amino acid; and

n is 0-100;

or a physiologically-acceptable salt thereof.

54. The method of Claim 53 wherein $Xaa_1$ is aspartic acid, glutamic acid, arginine, threonine, or α-hydroxymethylserine.

55. The method of Claim 53 wherein $Xaa_2$ is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or α-hydroxymethylserine.

56. The method of Claim 53 wherein $Xaa_3$ is lysine.

57. The method of Claim 53 wherein $Xaa_1$ is aspartic acid, glutamic acid, arginine, threonine, or α-hydroxymethylserine, $Xaa_2$ is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or α-hydroxymethylserine, and $Xaa_3$ is lysine.

58. The method of Claim 57 wherein $Xaa_1$ is aspartic acid or glutamic acid and $Xaa_2$ is alanine, glycine, valine, threonine, serine, leucine, or α-hydroxymethylserine.

59. The method of Claim 58 wherein $Xaa_2$ is alanine, threonine, leucine, or α-hydroxymethylserine.

60. The method of Claim 59 wherein $Xaa_1$ is aspartic acid and $Xaa_2$ is alanine.

61. The method of Claim 53 wherein n is 0-10.

62. The method of Claim 61 wherein n is 0-5.

63. The method of Claim 62 wherein n is 0.

64. The method of Claim 53 wherein $P_2$ comprises a metal-binding sequence.

65. The method of Claim 64 wherein $P_2$ comprises one of the following sequences:

$(Xaa_4)_m$ $Xaa_3$ His $Xaa_2$ $Xaa_5$,

$(Xaa_4)_m$ His $Xaa_2$ $Xaa_5$,

$(Xaa_4)_m$ $Xaa_5$ $Xaa_2$ His $Xaa_3$, or

$(Xaa_4)_m$ $Xaa_5$ $Xaa_2$ His,

wherein $Xaa_5$ is an amino acid having a free side-chain $-NH_2$ and m is 0-5.

66. The method of Claim 65 wherein $Xaa_5$ is Orn or Lys.

67. The method of Claim 64 wherein $P_2$ comprises one of the following sequences:

$[(Xaa_4)_mXaa_5Xaa_2HisXaa_3]_r$,

$[(Xaa_4)_mXaa_5Xaa_2His]_r$,

$[(Xaa_4)_mXaa_5Xaa_2HisXaa_3(Xaa_4)_mXaa_5Xaa_2His]_r$, or

$[(Xaa_4)_mXaa_5Xaa_2His(Xaa_4)_mXaa_5Xaa_2HisXaa_3]_r$,

wherein $Xaa_5$ is an amino acid having a free side-chain $-NH_2$, m is 0-5 and r is 2-100.

68. The method of Claim 64 wherein $P_2$ comprises a sequence which binds Cu(I).

69. The method of Claim 68 wherein $P_2$ comprises one of the following sequences:

Met $Xaa_4$ Met,

Met $Xaa_4$ $Xaa_4$ Met,

Cys Cys,

Cys $Xaa_4$ Cys,

Cys $Xaa_4$ $Xaa_4$ Cys,

Met $Xaa_4$ Cys $Xaa_4$ $Xaa_4$ Cys,

Gly Met $Xaa_4$ Cys $Xaa_4$ $Xaa_4$ Cys [SEQ ID NO:7],

Gly Met Thr Cys $Xaa_4$ $Xaa_4$ Cys [SEQ ID NO:8],

Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9], or

γ-Glu Cys Gly.

70. The method of Claim 69 wherein $P_2$ is Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9].

71. The method of Claim 53 wherein $P_2$ comprises a sequence which enhances the ability of the peptide to penetrate cell membranes, reach target tissues, or both.

72. The method of Claim 71 wherein $P_2$ is hydrophobic or an arginine oligomer.

73. The method of Claim 53 wherein at least one of the amino acids of $P_1$ other than β-alanine, when present, is a D-amino acid.

74. The method of Claim 73 wherein $Xaa_1$ is a D-amino acid, His is a D-amino acid, or both $Xaa_1$ and His are D-amino acids.

75. The method of Claim 74 wherein all of the amino acids of $P_1$ other than β-alanine, when present, are D-amino acids.

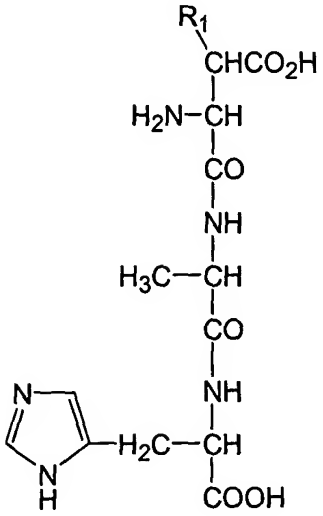
76. The method of Claim 73 wherein at least 50% of the amino acids of $P_2$ are D-amino acids.

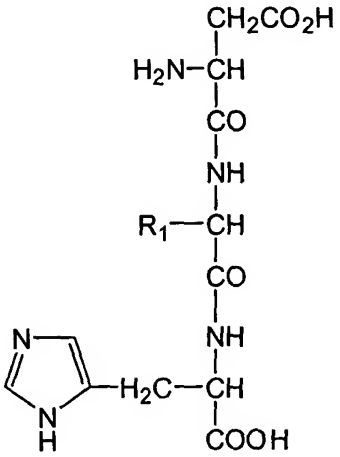
77. The method of Claim 74 wherein at least 50% of the amino acids of $P_2$ are D-amino acids.

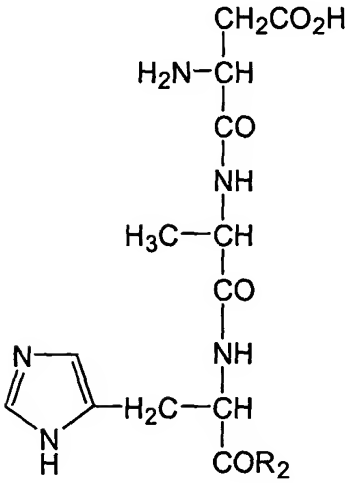
78. The method of Claim 75 wherein at least 50% of the amino acids of $P_2$ are D-amino acids.

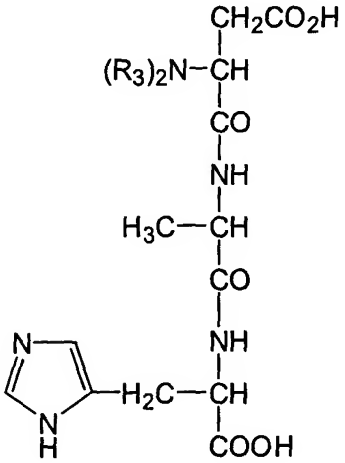
79. The method of Claim 53 wherein at least one amino acid of $P_1$, at least one amino acid of $P_2$, or at least one amino acid of $P_1$ and at least one amino acid of $P_2$, is substituted with (a) a substituent that increases the lipophilicity of the peptide without altering the ability of $P_1$ to bind metal ions, (b) a substituent that protects the peptide from proteolytic enzymes without altering the ability of $P_1$ to bind metal ions, or (c) a substituent which is a non-peptide, metal-binding functional group that improves the ability of the peptide to bind metal ions.

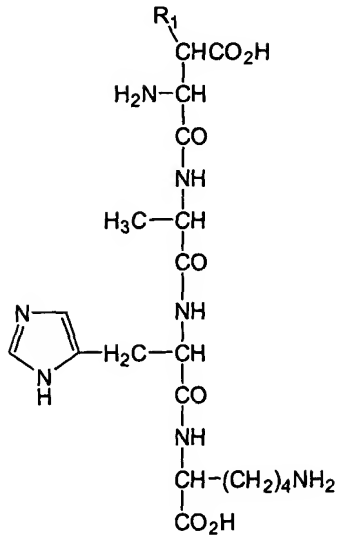
80. The method of Claim 79 wherein n is 0 and $P_1$ has one of the following formulas:

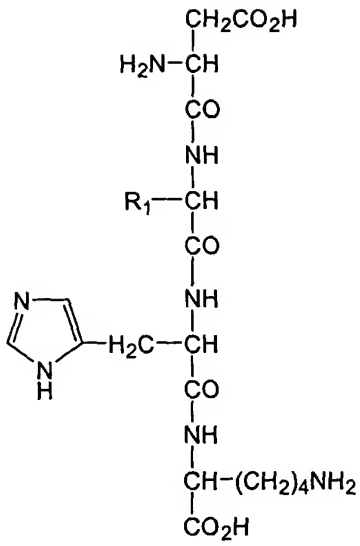


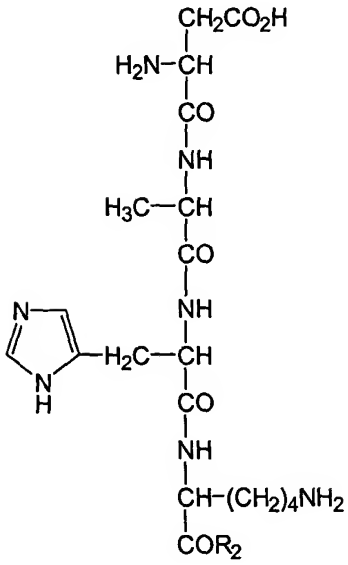


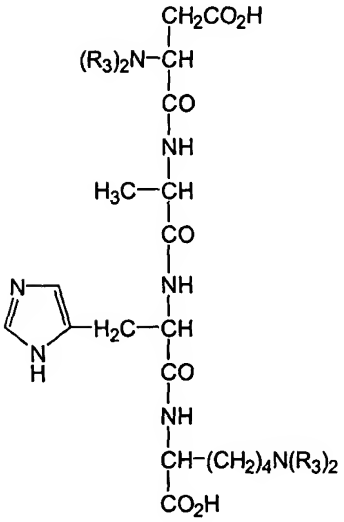












wherein:

$R_1$ is an alkyl, aryl, or heteroaryl;

$R_2$ is $-NH_2$, $-NHR_1$, $N(R_1)_2$, $-OR_1$, or $R_1$; and

$R_3$ is H, a non-peptide, metal-binding functional group or the two $R_3$ groups together form a non-peptide, metal-binding functional group.

81. The method of Claim 53 wherein the solution of medium further comprises an effective amount of another metal-binding compound in combination with the peptide.

82. The method of Claim 53 wherein the cell, tissue or organ is transplanted into an animal after being contacted with the solution or medium containing the peptide.

83. A method of reducing the concentration of a metal in an animal in need thereof comprising administering to the animal an effective amount of a peptide having the formula:

$$P_1 - P_2,$$

wherein:

$P_1$ is:

$Xaa_1$ $Xaa_2$ His: or

$Xaa_1$ $Xaa_2$ His $Xaa_3$;

$P_2$ is $(Xaa_4)_n$;

$Xaa_1$ is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_2$ is glycine, alanine, β-alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_3$ is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

$Xaa_4$ is any amino acid; and

n is 0-100;

or a physiologically-acceptable salt thereof.

119. A method of reducing the damage done by reactive oxygen species (ROS) in an animal comprising administering to the animal an effective amount of a metal-binding peptide having attached thereto a non-peptide, metal-binding functional group.

124. A method of reducing the damage done by reactive oxygen species (ROS) to a cell, a tissue or an organ that has been removed from an animal comprising contacting the cell, tissue or organ with a solution or medium containing an effective amount of a metal-binding peptide having attached thereto a non-peptide, metal-binding functional group.

129. A method of reducing the concentration of metal in an animal in need thereof comprising administering to the animal an effective amount of a metal-binding peptide having attached thereto a non-peptide, metal-binding functional group.

134. A method of reducing the damage done by reactive oxygen species (ROS) in an animal comprising administering to the animal an effective amount of a metal-binding peptide dimer of the formula:

$$P_3 - L - P_3,$$

wherein:

each $P_3$ may be the same or different and is a peptide which is capable of binding a metal ion; and

L is a chemical group which connects the two $P_3$ peptides through their C-terminal amino acids.

158. A method of reducing the damage done by reactive oxygen species (ROS) to a cell, a tissue or an organ that has been removed from an animal comprising contacting the

cell, tissue or organ with a solution or medium containing an effective amount of a metal-binding peptide dimer of the formula:

$$P_3 - L - P_3,$$

wherein:

each $P_3$ may be the same or different and is a peptide which is capable of binding a metal ion; and

L is a chemical group which connects the two $P_3$ peptides through their C-terminal amino acids.

182. A method of reducing the concentration of a metal in an animal in need thereof comprising administering to the animal an effective amount of a metal-binding peptide dimer of the formula:

$$P_3 - L - P_3,$$

wherein:

each $P_3$ may be the same or different and is a peptide which is capable of binding a metal ion; and

L is a chemical group which connects the two $P_3$ peptides through their C-terminal amino acids.

206. A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and a peptide having the formula:

$$P_1 - P_2,$$

wherein:

$P_1$ is:

$Xaa_1\ Xaa_2$ His: or

$Xaa_1\ Xaa_2$ His $Xaa_3$;

$P_2$ is $(Xaa_4)_n$;

$Xaa_1$ is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_2$ is glycine, alanine, β-alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_3$ is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

$Xaa_4$ is any amino acid; and

n is 0-100;

or a physiologically-acceptable salt thereof.

234. A kit comprising a container holding a peptide having the formula:

$$P_1 - P_2,$$

wherein:

$P_1$ is:

$Xaa_1\ Xaa_2$ His: or

$Xaa_1\ Xaa_2$ His $Xaa_3$;

$P_2$ is $(Xaa_4)_n$;

$Xaa_1$ is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_2$ is glycine, alanine, β-alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_3$ is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

$Xaa_4$ is any amino acid; and

n is 0-100;

or a physiologically-acceptable salt thereof.

235. The kit of Claim 234 wherein $Xaa_1$ is aspartic acid, glutamic acid, arginine, threonine, or α-hydroxymethylserine.

236. The kit of Claim 234 wherein $Xaa_2$ is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or α-hydroxymethylserine.

237. The kit of Claim 234 wherein $Xaa_3$ is lysine.

238. The kit of Claim 234 wherein $Xaa_1$ is aspartic acid, glutamic acid, arginine, threonine, or α-hydroxymethylserine, $Xaa_2$ is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or α-hydroxymethylserine, and $Xaa_3$ is lysine.

239. The kit of Claim 238 wherein $Xaa_1$ is aspartic acid or glutamic acid and $Xaa_2$ is alanine, glycine, valine, threonine, serine, leucine, or α-hydroxymethylserine.

240. The kit of Claim 239 wherein $Xaa_2$ is alanine, threonine, leucine, or α-hydroxymethylserine.

241. The kit of Claim 240 wherein $Xaa_1$ is aspartic acid and $Xaa_2$ is alanine.

242. The kit of Claim 234 wherein n is 0-10.

243. The kit of Claim 242 wherein n is 0-5.

244. The kit of Claim 243 wherein n is 0.

245. The kit of Claim 234 wherein $P_2$ comprises a metal-binding sequence.

246. The kit of Claim 245 wherein $P_2$ comprises one of the following sequences:

$(Xaa_4)_m\ Xaa_3\ His\ Xaa_2\ Xaa_5$,

$(Xaa_4)_m\ His\ Xaa_2\ Xaa_5$,

$(Xaa_4)_m\ Xaa_5\ Xaa_2\ His\ Xaa_3$, or

$(Xaa_4)_m\ Xaa_5\ Xaa_2\ His$,

wherein $Xaa_5$ is an amino acid having a free side-chain $-NH_2$ and m is 0-5.

247. The kit of Claim 246 wherein $Xaa_5$ is Orn or Lys.

248. The kit of Claim 245 wherein $P_2$ comprises one of the following sequences:

$[(Xaa_4)_mXaa_5Xaa_2HisXaa_3]_r$,

$[(Xaa_4)_mXaa_5Xaa_2His]_r$,

$[(Xaa_4)_mXaa_5Xaa_2HisXaa_3(Xaa_4)_mXaa_5Xaa_2His]_r$, or

$[(Xaa_4)_mXaa_5Xaa_2His(Xaa_4)_mXaa_5Xaa_2HisXaa_3]_r$,

wherein $Xaa_5$ is an amino acid having a free side-chain $-NH_2$, m is 0-5 and r is 2-100.

249. The kit of Claim 245 wherein $P_2$ comprises a sequence which binds Cu(I).

250. The kit of Claim 249 wherein $P_2$ comprises one of the following sequences:

Met $Xaa_4$ Met,

Met $Xaa_4$ $Xaa_4$ Met,

Cys Cys,

Cys $Xaa_4$ Cys,

Cys $Xaa_4$ $Xaa_4$ Cys,

Met $Xaa_4$ Cys $Xaa_4$ $Xaa_4$ Cys,

Gly Met $Xaa_4$ Cys $Xaa_4$ $Xaa_4$ Cys [SEQ ID NO:7],

Gly Met Thr Cys $Xaa_4$ $Xaa_4$ Cys [SEQ ID NO:8],

Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9], or

γ-Glu Cys Gly.

251. The kit of Claim 250 wherein $P_2$ is Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9].

252. The kit of Claim 234 wherein $P_2$ comprises a sequence which enhances the ability of the peptide to penetrate cell membranes, reach target tissues, or both.

253. The kit of Claim 252 wherein $P_2$ is hydrophobic or an arginine oligomer.

254. The kit of Claim 234 wherein at least one of the amino acids of $P_1$ other than β-alanine, when present, is a D-amino acid.

255. The kit of Claim 254 wherein $Xaa_1$ is a D-amino acid, His is a D-amino acid, or both $Xaa_1$ and His are D-amino acids.

256. The kit of Claim 255 wherein all of the amino acids of $P_1$ other than β-alanine, when present, are D-amino acids.

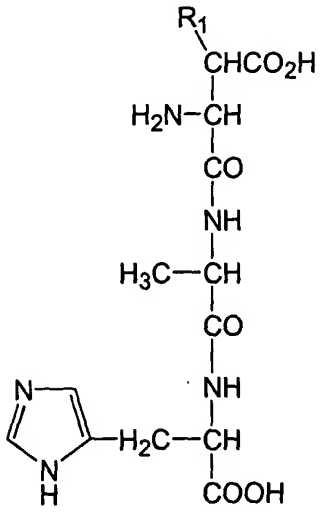
257. The kit of Claim 254 wherein at least 50% of the amino acids of $P_2$ are D-amino acids.

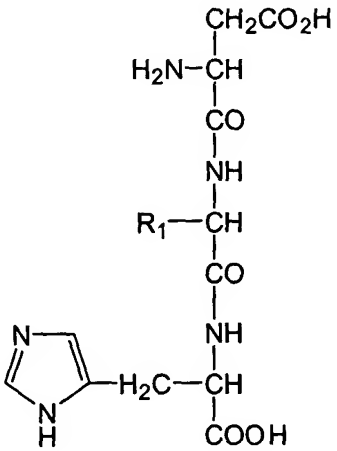
258. The kit of Claim 255 wherein at least 50% of the amino acids of $P_2$ are D-amino acids.

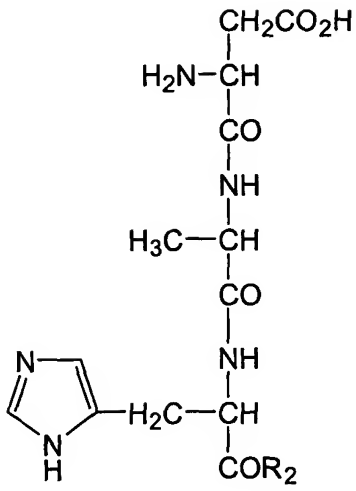
259. The kit of Claim 256 wherein at least 50% of the amino acids of $P_2$ are D-amino acids.

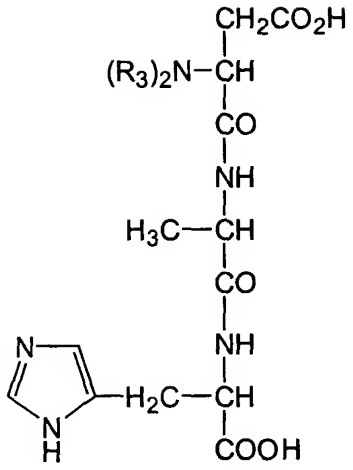
260. The kit of Claim 234 wherein at least one amino acid of $P_1$, at least one amino acid of $P_2$, or at least one amino acid of $P_1$ and at least one amino acid of $P_2$ is substituted with (a) a substituent that increases the lipophilicity of the peptide without altering the ability of $P_1$ to bind metal ions, (b) a substituent that protects the peptide from proteolytic enzymes without altering the ability of $P_1$ to bind metal ions, or (c) a substituent which is a non-peptide, metal-binding functional group that increases the ability of the peptide to bind metal ions.

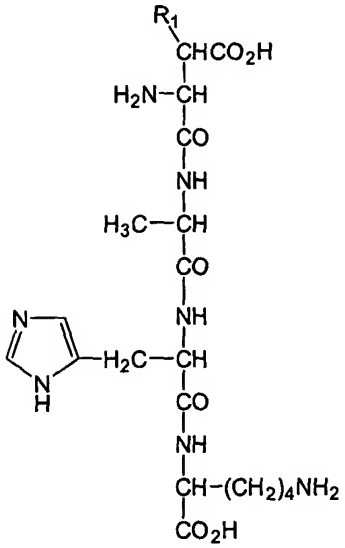
261. The kit of Claim 260 wherein n is 0 and $P_1$ has one of the following formulas:

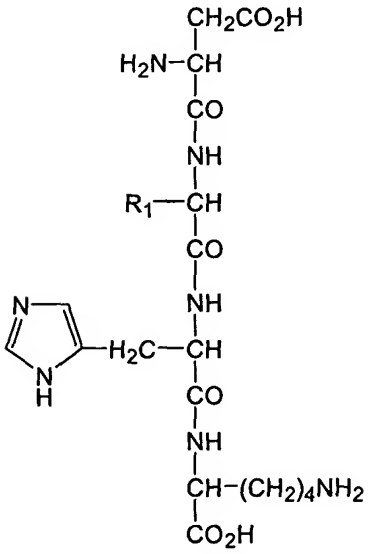


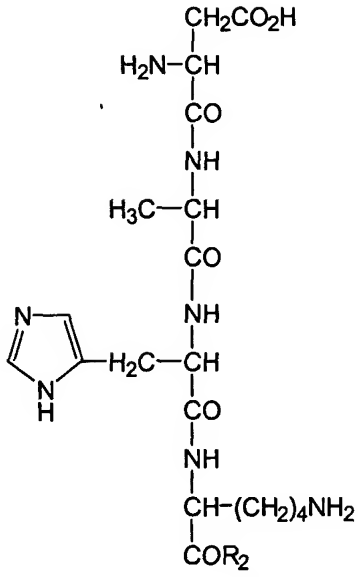


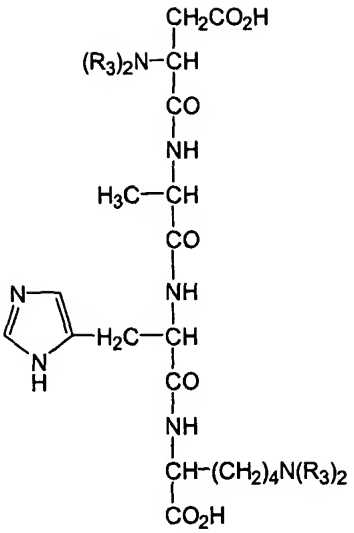












wherein:

$R_1$ is an alkyl, aryl, or heteroaryl;

$R_2$ is $-NH_2$, $-NHR_1$, $N(R_1)_2$, $-OR_1$, or $R_1$; and

$R_3$ is H, a non-peptide, metal-binding functional group or the two $R_3$ groups together form a non-peptide, metal-binding functional group.

262. A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and a metal-binding peptide having attached thereto a non-peptide, metal-binding functional group.

266. A kit comprising a container holding a metal-binding peptide having attached thereto a non-peptide, metal-binding functional group.

270. A composition comprising a metal-binding peptide dimer of the formula:

$P_3 - L - P_3$,

wherein:

each $P_3$ may be the same or different and is a peptide which is capable of binding a metal ion; and

L is a chemical group which connects the two $P_3$ peptides through their C-terminal amino acids.

293. A kit comprising a container holding a metal-binding peptide dimer of the formula:

$$P_3 - L - P_3,$$

wherein:

each $P_3$ may be the same or different and is a peptide which is capable of binding a metal ion; and

L is a chemical group which connects the two $P_3$ peptides through their C-terminal amino acids.

316. A peptide having the formula:

$$P_1 - P_2,$$

wherein:

$P_1$ is:

$Xaa_1\ Xaa_2$ His: or

$Xaa_1\ Xaa_2$ His $Xaa_3$;

$P_2$ is $(Xaa_4)_n$;

$Xaa_1$ is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_2$ is glycine, alanine, β-alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_3$ is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

$Xaa_4$ is any amino acid;

n is 0-100; and

at least one amino acid of $P_1$ is a D-amino acid;

or a physiologically-acceptable salt thereof.

343. A peptide having the formula:

$$P_1 - P_2,$$

wherein:

$P_1$ is:

$Xaa_1$ $Xaa_2$ His: or

$Xaa_1$ $Xaa_2$ His $Xaa_3$;

$P_2$ is $(Xaa_4)_n$;

$Xaa_1$ is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_2$ is glycine, alanine, β-alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_3$ is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

$Xaa_4$ is any amino acid;

n is 0-100; and

at least one amino acid of $P_1$, at least one amino acid of $P_2$, or at least one amino acid of $P_1$ and at least one amino acid of $P_2$ is substituted with (a) a substituent that increases the lipophilicity of the peptide without altering the ability of $P_1$ to bind metal ions, (b) a

substituent that protects the peptide from proteolytic enzymes without altering the ability of $P_1$ to bind metal ions, or (c) a substituent which is a non-peptide, metal-binding functional group that improves the ability of the peptide to bind metal ions.;

or a physiologically-acceptable salt thereof.

370. A metal-binding peptide having the formula:

$$P_1 - P_2,$$

wherein:

$P_1$ is:

$Xaa_1$ $Xaa_2$ His: or

$Xaa_1$ $Xaa_2$ His $Xaa_3$;

$P_2$ is a peptide sequence which comprises the sequence of a metal binding site;

$Xaa_1$ is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_2$ is glycine, alanine, β-alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine; and

$Xaa_3$ is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

or a physiologically-acceptable salt thereof.

392. A metal-binding peptide dimer of the formula:

$$P_3 - L - P_3,$$

wherein:

each $P_3$ may be the same or different and is a peptide which is capable of binding a metal ion; and

L is a chemical group which connects the two $P_3$ peptides through their C-terminal amino acids.

415. A method of *in vitro* fertilization wherein a medium is utilized which comprises an amount of a peptide effective to reduce the damage done by reactive oxygen species, the peptide having the formula:

$$P_1 - P_2,$$

wherein:

$P_1$ is:

$Xaa_1$ $Xaa_2$ His: or

$Xaa_1$ $Xaa_2$ His $Xaa_3$;

$P_2$ is $(Xaa_4)_n$;

$Xaa_1$ is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_2$ is glycine, alanine, β-alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α-hydroxymethylserine;

$Xaa_3$ is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

$Xaa_4$ is any amino acid; and

n is 0-100;

or a physiologically-acceptable salt thereof.

417. A method of *in vitro* fertilization wherein a medium is utilized which comprises an amount of a metal-binding peptide effective to reduce the damage done by reactive

oxygen species, the metal-binding peptide having attached thereto a non-peptide, metal-binding functional group.

418. A method of *in vitro* fertilization wherein a medium is utilized which comprises an amount of a metal-binding peptide dimer effective to reduce the damage done by reactive oxygen species, the peptide dimer having the formula:

$$P_3 - L - P_3,$$

wherein:

each $P_3$ may be the same or different and is a peptide which is capable of binding a metal ion; and

L is a chemical group which connects the two $P_3$ peptides through their C-terminal amino acids.